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ORIGINAL ARTICLE

Role of soluble intercellular adhesion molecule-1 in the process of peritonitis in peritoneal dialysis

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Abstract

Objective: To investigate the role and clinical significance of changes of levels of soluble intercellular adhesion molecule-1 in the process of peritonitis in peritoneal dialysis patients.

Methods: A total of 50 patients on continuous ambulatory peritoneal dialysis in the Shanghai Changhai Hospital between May 1999 and July 2000 were enrolled into this study. They were assigned to two groups according to diagnostic standard of peritonitis—Group A, with episodes of peritonitis; Group B, in the absence of peritonitis. The serum and peritoneal effluent levels of soluble intercellular adhesion molecule-1 during and after peritonitis were assessed by using sandwiched enzyme-linked immunosorbent assay.

Results: The serum levels of soluble intercellular adhesion molecule-1 in Group A were significantly lower compared with Group B (214.5 ± 90.7 vs 511.2 ± 124.7 ng/mL; p<0.01). The peritoneal effluent levels of soluble intercellular adhesion molecule-1 in Group A were significantly higher than those in Group B (5.8 ± 1.6 vs 2.1 ± 0.9 ng/mL; p<0.01). For Group A, after treatment of peritonitis, the serum levels of soluble intercellular adhesion molecule-1 profoundly increased to 506.1 ± 107.8 ng/mL and the peritoneal effluent levels of soluble intercellular adhesion molecule-1 markedly decreased to 3.9 ± 1.1 ng/mL, compared with those during peritonitis, respectively (p<0.01).

Conclusion: The study showed that increased peritoneal effluent levels of soluble intercellular adhesion molecule-1 during peritonitis possibly activate or damage peritoneal mesothelial cells. Monitoring changes of levels of soluble intercellular adhesion molecule-1 in peritoneal dialysis fluid may be useful for analyzing the process of peritonitis.

Key words: Cell adhesion, Enzyme-linked immunosorbent assay, Integrins, Leukocytes/physiology, Molecular structure

中文摘要

目的：探討可溶性細胞間粘附分子-1（soluble intercellular adhesion molecule-1, sICAM-1）水平的變化在腹膜透析患者腹膜炎過程中的作用及意義。

方法：共50例於1999年5月至2001年7月在上海長海醫院進行連續性家居腹膜透析的患者被納入本研究。根據腹膜炎的診斷標準分組——A組：存在腹膜炎的發生；B組，無腹膜炎的發生。採用夾心酶聯免疫吸附法分別檢測兩組患者的血清及腹膜透出液中sICAM-1水平的變化。

結果：A組患者血清sICAM-1水平（214.5 ± 90.7 ng/mL）與B組患者（511.2 ± 124.7 ng/mL）相比顯著降低（$p < 0.01$），而腹膜透出液sICAM-1水平則顯著增加（5.8 ± 1.6 vs 2.1 ± 0.9 ng/mL; $p < 0.01$）。

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A組患者腹膜炎治療三周後，血清及透出液 sICAM-1 水平分別為 506.1 ± 107.8 及 3.9 ± 1.1 ng/mL，與腹膜炎發生時期相比分別顯著增加及降低（$p < 0.01$）。

結論：腹膜炎患者的腹透液中sICAM-1水平的升高，可能在一定程度上反映了炎症過程中腹膜間皮細胞的激活及損害，從而推測監測腹膜透出液中 sICAM-1 水平的變化可能有助於瞭解腹膜炎的發展過程。

INTRODUCTION

Adhesion molecules are a heterogeneous group of ligand/receptor molecules that mediate cell adhesion either to other cells or to the extracellular matrix. Cell adhesion is of fundamental importance to many processes, including cell differentiation and organization in tissues (1), recirculation and migration of leukocytes (2), activation and intercommunication of immune cells (3), and growth and metastasis of tumor cells (4). Adhesion molecules can be separated into three main groups on the basis of molecular, structural, and functional differences: the immunoglobulin family, which includes intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), the integrin family, and the selectins (P-selectin, L-selectin, and E-selectin).

In addition to being expressed on the surface of various cells (mainly endothelial cells and circulating blood cells such as leukocytes and platelets), adhesion molecules can be detected as soluble forms in the circulation (5,6). Circulating soluble adhesion molecules seem to be biologically active, and increased levels have been reported in several conditions, including septic shock, diabetes, atherosclerosis, vasculitis, and Grave's disease (7,8).

Peritonitis is a major cause of mortality and morbility in peritoneal dialysis (9). Because an impaired immune system is related to the occurrence of peritonitis, the aim of this study was to measure the serum and peritoneal effluent levels of soluble ICAM-1 (sICAM-1) in patients on long-term continuous ambulatory peritoneal dialysis (CAPD), including episodes of peritonitis and absence of peritonitis, and study the relationships between changing levels of sICAM-1 and peritonitis.

METHODS

A total of 50 CAPD patients who received dialysis in the Changhai hospital between May 1999 and July 2001 were enrolled into this study. According to the diagnostic standard of peritonitis, these patients were divided into two groups: 1. patients with episodes of peritonitis (Group A), in which the peritonitis rate was one per 16 patient-months; and 2. patients in absence of peritonitis (Group B), who never had peritonitis during the follow-up periods. The standard treatment for CAPD peritonitis was continuous intraperitoneal cefazolin plus tobramycin for 21 days.

Blood samples and peritoneal effluents of the overnight dwell were obtained from these patients. For Group A, both blood samples and peritoneal effluents, including the moment the diagnosis of peritonitis was made and after 21 days of treatment of peritonitis, were also obtained. Concentrations for sICAM-1 were determined by enzyme-linked immunosorbent assay using standard kits (Sigma Corp.). The concentration of sICAM-1 was estimated with reference to standard curves performed with the corresponding recombinant molecules.

All data are expressed as mean ± standard deviation. Statistical analysis was performed using the package Statistica for Windows, version 3.1. Comparisons between groups were performed using Student's *t* test. A *p* value of less than 0.05 was considered significant.

RESULTS

A follow-up was conducted on all 50 CAPD patients for 19.5 ± 3.7 months. There were 27 men and 23 women, and their mean age was 55.2 ± 8.2 years. Background demographic data of the two groups defined by the diagnostic standard of peritonitis are compared in Table 1. There was no significant difference between the two groups ($p>0.05$).

The serum levels of sICAM-1 in Group A were significantly lower than those in Group B (214.5 ± 90.7 vs 511.2 ± 124.7 ng/mL, respectively; $p<0.01$). The peritoneal effluent levels of sICAM-1 were significantly higher than those in Group B (5.8 ± 1.6 vs 2.1 ± 0.9 ng/mL,

Table 1. Background demographic data of the two groups defined by the diagnostic standard of peritonitis.

	Group A	Group B
No. of cases	24	26
Sex ratio (M/F)	15:9	19:7
Age, years	54.3 ± 6.5	56.9 ± 9.2
Underlying renal diagnosis		
Glomerulonephritis	11	17
Hypertension	5	2
Diabetes	1	3
Polycystic	3	1
Other/unknown	4	3
Duration of PD, months	18.8 ± 2.7	20.7 ± 4.3

PD = peritoneal dialysis

respectively; $p<0.01$). For Group A, after treatment of peritonitis, the serum levels of sICAM-1 (506.1 ± 107.8 ng/mL) significantly increased compared with those during peritonitis ($p<0.01$), whereas the peritoneal effluent levels of sICAM-1 (3.9 ± 1.1 ng/mL) markedly decreased compared with those during peritonitis ($p<0.01$).

DISCUSSION

There is increasing interest in the soluble forms of adhesion molecules. It is thought that they may be involved in leukocyte-endothelial cell interaction because their ligands are present on circulating leukocytes, and there may be a role for these molecules in acute and/or chronic inflammation, in atherosclerosis, and connective tissue diseases (10,11). Findings also indicate that increased levels of circulating molecules such as sICAM-1 could protect from autoimmunity (12).

In this study, we found that the peritoneal effluent levels of sICAM-1 were significantly higher in Group A than in Group B. The mechanism responsible for this can only be speculative for the moment. During peritonitis, cytokines stimulation, such as interleukin-1 or tumor necrosis factor-α, can mediate and upregulate the expression of ICAM-1 on the surface of peritoneal mesothelial cells, which is followed by the release of sICAM-1 by proteolytic cleavage at or near the cellular membrane without cell necrosis occurring (13). It is therefore possible that cytokines may contribute to the increased peritoneal effluent levels of sICAM-1 in CAPD peritonitis patients by promoting the production of sICAM-1 molecules. Meanwhile, we found that the serum levels of sICAM-1 profoundly decreased in these patients. However, the reason for it cannot be explained with present knowledge.

The clinical significance of increased levels of circulating adhesion molecules is unclear (14,15). The precise source of the increases in soluble molecules will considerably aid the interpretation of these findings. Membrane-bound ICAM-1 are found on peritoneal mesothelial cells and a diverse range of other cell types (16), but the cellular source for sICAM-1 *in vivo* still has not been definitively established. The circulating levels of these molecules may be regarded as markers for the extent of an inflammatory process, as suggested in particular for sICAM-1, or for peritoneal mesothelium damage, or both. The present study showed that the increased peritoneal effluent levels of sICAM-1 were corrected after treatment of peritonitis, which seems to reveal a correlation between changes of levels of sICAM-1 and the process of peritonitis. However, the physiological role of adhesion molecules has yet to be fully clarified.

In conclusion, increased peritoneal effluent levels of sICAM-1 during CAPD peritonitis suggest the possibility of peritoneal mesothelial cell activation or damage, and it has also been suggested that peritoneal mesothelial cells are subject to inflammatory stimuli. The finding may lead to more understanding of the process of peritonitis. The clinical use of monitoring changes of peritoneal effluent levels of sICAM-1 during peritonitis remains to be elucidated.

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